REMARKS

Claims 2-11 and 13-22 were pending. Claims 6, 11, 17 and 22 are cancelled by the present amendment, and claims 13 and 15 are amended. Accordingly, claims 2-5, 7-10, 13-16 and 18-21 are pending and presented for reconsideration.

Claim 13 is amended to recite lipopolysaccharide (LPS)-induced bacterial translocation. Support for the amendment to claim 13 is found in the originally-filed application at least, for example, at pages 8 and 9 and in Figure 2.

Claims 4 and 15 are amended to recite that the TCF-II is produced recombinantly. Support for the amendment to claim 15 is found in the originally-filed application at least, for example, at pages 5 and 6.

Applicants submit that the amendments introduce no new matter.

Telephonic interview

Applicants thank Examiner Duffy for the telephonic interview of March 5, 2003. Applicants have attempted, in this paper, to reflect the substance of the telephonic interview, and believe that all pending claims are now in condition for allowance.

Election/Restriction

According to the Office action, 1) claims 2-23 were pending in the application, and 2) a complete reply to the restriction requirement must include cancellation of nonelected claims 12 and 23. Applicants submit that claims 12 and 23 were cancelled by the Amendment and Response filed September 23, 2002.

Claim rejections under 35 U.S.C. § 112

Claims 4 and 15 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter insufficiently described in the specification.

According to the Office action: "This issue may be resolved by applicants amending the claim to state that 'the TCF-II is produced recombinantly.'" Applicants have cancelled claim 4 and amended claim 15 to recite that the TCF-II is produced recombinantly. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 2-11 and 13-22 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabling the full scope of the claims. The Office action acknowledged that the specification enables "a method of increasing the survival rate of sepsis in a mammal by decreasing lipopolysaccharide (LPS)-induced bacterial translocation in the intestine comprising administering to the mammal an amount of isolated or purified tissue cytotoxic factor – II (TCF-II) sufficient to decrease LPS-induced bacterial translocation in the intestine thereby increasing the survival rate of sepsis." Applicants have amended independent claim 13 to recite a method of reducing LPS-induced bacterial translocation in a mammal, comprising administering an amount of isolated or purified TCF-II effective to reduce LPS-induced bacterial translocation. Accordingly, Applicants submit that indepenent claim 13 and all claims depending on claim 13 are allowable.

Applicants further submit that independent claim 2 and its dependent claims are allowable. In Example 1, Applicants have demonstrated that TCF-II administration significantly increases survival in rats made septic by puncture of the cecum. As discussed in Wichterman *et al.*, (1980) J. Surg. Res. 29:189-201, a copy of which is attached as Exhibit A, puncture of the cecum causes an "immediate and constant leakage of bacteria into the peritoneal cavity" (Wichterman, p.195). Applicants do not argue that TCF-II prevents the immediate and constant leakage of bacteria, but instead submit that TCF-II reduces lethality associated with bacterial invasion. Accordingly, Applicants submit that the application enables methods for reducing sepsis-associated lethality that are not limited to a particular route of bacterial invasion or to a particular trigger of sepsis (*e.g.* burns, surgery, *etc.*), and that claim 2 and all claims depending on claim 2 are allowable.

Claims 2 and 22 stand rejected under 35 U.S.C. § 112, second paragraph. Applicants believe the Office action intended to refer not to claims 2 and 22, but to claims 11 and 22. Claims 11 and 22 have been cancelled. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

CONCLUSION

Claims 2-5, 7-10, 13-16 and 18-21 are pending and presented for consideration. The Examiner is encouraged to contact the undersigned to discuss any outstanding issues.

Respectfully submitted,

Brian A. Fairchild, Ph.D.
Agent for the Applicant
Testa, Hurwitz & Thibeault, LLP
High Street Tower
125 High Street
Boston, MA 02110

Date: March 12, 2003
Reg. No. 48,645
Tel. No.: (617) 248-7697
Fax No.: (617) 248-7100

MARKED-UP COPY OF THE AMENDED CLAIMS

4. (Amended) The method of claim 2, wherein the TCF-II is produced recombinantly [comprising the additional step, prior to step (a), of

expressing a recombinant DNA encoding TCF-II in a host cell, thereby to prepare the therapeutic agent].

13. (Twice Amended) A method for reducing lipopolysaccharide (LPS)-induced bacterial translocation in a mammal, the method comprising the step of:

(a) administering to a mammal at risk of LPS-induced bacterial translocation in the intestine an amount of isolated or purified tissue cytotoxic factor – II (TCF-II) effective to reduce LPS-induced bacterial translocation.

15. (Amended) The method of claim 13, wherein the TCF-II is produced recombinantly [comprising the additional step, prior to step (a), of

expressing a recombinant DNA encoding TCF-II in a host cell, thereby to prepare the therapeutic agent].